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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Norman Nashed

Serial No. 09/619,493 : Examiner: S. Qazi

Filed: July 19, 2000 : Group Art Unit: 1616

Title: **THERAPEUTIC GESTAGENS FOR THE TREATMENT OF PREMENSTRUAL DYSPHORIC DISORDER**

DECLARATION UNDER 37 C.F.R. §1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Carole Sampson-Landers, being duly warned declared that:

I am a citizen of the United States, residing at 6 Deer Run, Lebanon, NJ.

I possess the degrees of B.A., M.M.S. and M.D, having studied at Douglass College, Rutgers Medical School and Temple University Medical School.

I am a member of American Medical Women's Association and Drug Information Association.

I have been employed as Medical Director of Clinical Development in Female Health Care at Berlex Laboratories in Montville, NJ since April 2002.

I am a regional medical expert and local clinical team leader for ongoing Phase 2/3 clinical trials for new indications in female health.

I, Marie L. Foegh, being duly warned declared that:

I am a citizen of the United States, residing at 44 Adams Drive, Cresskill, NJ.

I possess the degrees of M.D. and D.Sc., having studied at University of Copenhagen Medical School, Copenhagen Denmark. I did postgraduate training at University Hospitals and the University Department OB/GYN at Frederiksberg

Hospital in Copenhagen, Denmark. I also held a fellowship in the Department of Medicine at Georgetown University Medical Center, Washington, D.C.
I am currently a Clinical Professor of Medicine at Emory University Medical School in the Department of OB/GYN and Vice President of Female Healthcare in Clinical Research at Berlex Laboratories in Montville, NJ.

It is understood and recognized by researchers and practitioners in the field of obstetrics and gynecology that PMS (premenstrual syndrome) and PMDD (premenstrual dysphoric disorder), while sharing some of the same signs and symptoms, have important and distinguishable differences.
PMDD usually comprises extremely distressing emotional and behavioral symptoms including irritability, dysphoria, tension, and mood liability which may be accompanied by physical complaints. It appears 3 to 10 days prior to the onset of menstrual bleeding and remits after menses. The symptoms of PMDD are severe enough to impair social and occupational functioning. Approximately 3-8% of women of reproductive age are affected (Steiner, M. and Born, L. (2000) *Inter. Clin. Psychopharmacology*; 15 (suppl 3): S15-S17).

PMDD has a distinct clinical picture wherein the symptoms include irritability, anger, and tension and the physical symptoms which include breast tenderness and bloating are unique. Also, gonadal hormone suppression has been used to relieve symptoms and serotonergic antidepressants can be used for treatment.

PMS affects approximately 75% of women of reproductive age and the symptoms appear in the luteal phase and cease with menses. There are neither functional impairments nor specific charting requirements. Typical treatment for PMS patients consists of a non-pharmacologic approach including conservative modalitites such as lifestyle changes, stress management, diet, exercise, nutritional supplements, and cognitive/behavioral therapy.

PMDD can be distinguished from PMS by using the American Psychiatric Association definition which describes PMDD as having at least five of the following symptoms: sadness, anxiety, mood swings, persistent irritability, withdrawal, difficulty concentrating, fatigue, marked changes in appetite and sleep patterns, a feeling of being overwhelmed; and as such physical symptoms as headache, joint and muscle pain, weight gain and bloating. The symptoms must be prospectively documented for two consecutive menstrual cycles with at least 50% change in symptom severity between the luteal and follicular phases (Steiner, M. et al. (1995) *New England J. Medicine*; 332:1529-1534) and PMS, by contrast, is described as having only one of the above-mentioned symptoms restricted to the luteal phase of the menstrual cycle.

PMDD is principally differentiated from PMS on the basis of functional impairment and response to pharmacological treatment. PMS is not associated with PMDD. PMDD responds to pharmacologic treatment whereas PMS does not.

A summary of the key identifiers for distinguishing PMDD from PMS is shown below in Table 1.

Table 1. PMDD v. PMS

	PMDD	PMS
Clearly linked to menstrual cycle	X	X
Sufficient distress to seek medical treatment	X	X
Symptoms not due to another disorder	X	X
Symptoms confirmed by daily ratings	X	X
Symptoms interfere with functioning	X	
5 of 11 specified symptoms required	X	
Diagnosis recognized by FDA	X	
Responds to pharmacologic treatment	X	

In view of the evidence collected to date, experts in women's health care have

reached a clear consensus that PMDD is a distinct clinical entity (see e.g. *J. of Women's Health & Gender-Based Medicine* (1999), Vol.8, Number 5, pages 663-679).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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